

REMARKS

Amendments to the Claims

Claims 1-7 are pending in the application. Claim 1 has been amended. Support for amendments to Claim 1 can be found, for example, on page 15 lines 25-28; page 25 lines 25-30; page 26 lines 23-31; page 27 lines 26-31; page 29 line 19-page 31 line 10; page 33 lines 8-19; page 43; and pages 77-78 of the specification as filed. No new matter has been added.

Claim Rejection under 35 U.S.C. § 112, ¶2

Claim 1 has been amended in accordance with the Examiner's suggestion to remove the term "substantially" from the claim. Applicant thus respectfully requests the Examiner's rejection be withdrawn.

Rejection of Claims under 35 U.S.C. § 103(a)

Claims 1, 2 and 4-6 are rejected under 35 U.S.C. §103(a) as obvious in light of U.S. Pat. No. 5,437,982 to Catterall et al. ("Catterall") in view of Connolly et al., Biosensors and Bioelectronics, 1990 5: 223-234 ("Connolly").

Independent Claim 1 has been amended to recite, inter alia, modulating a transmembrane potential of cells with a series of electric field pulses "so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of [a] target ion channel, wherein the frequency of the electric field pulses (f) is within the range $\tau_M^{-1} \leq f \leq \tau_b^{-1}$ where τ_M is a time constant for decay of transmembrane potential changes, and τ_b is an average target ion channel open time wherein the pulses at said frequency cause a gradual change in transmembrane potential over the course of said series of pulses."

Catterall does not teach applying pulses at a rate that causes a gradual change in transmembrane potential over the course of the series of pulses as recited in Claim 1. Because Catterall uses a patch clamp, the transmembrane potential will follow the pulse amplitude up and down with each applied pulse regardless of their rate. The potential will not change gradually over the course of the series of electric fields pulses.

Similarly, Connolly does not teach using a pulse frequency to cause a gradual change in transmembrane potential over the course of the pulses. Connolly discloses stimulation of cardiac

myocyte cells using a “slow (1 Hz) biphasic square wave applied to the stimulating electrode. . . . If beating commenced [in the cardiac cells] then the removal of the stimulus did not cause its cessation.” See Connolly at page 232. Thus, Connolly also does not disclose modulating a cell transmembrane potential “wherein the frequency of the electric field pulses (f) is within the range $\tau_M^{-1} \leq f \leq \tau_b^{-1}$ where τ_M is a time constant for decay of transmembrane potential changes, and τ_b is an average target ion channel open time, wherein the pulses at said frequency cause a change from a starting transmembrane potential to said set transmembrane potential over the course of said series of pulses.” Thus, the combination of Catterall and Connolly does not teach all of the elements of amended Claim 1.

The applicant wishes to emphasize that stimulation with extracellular electrodes has dramatically different effects from patch clamping. The Examiner’s assertion that Connolly points out that extracellular electrodes are a suitable substitute for an intracellular patch clamp is not accurate. Just because extracellular electrodes can initiate beating does not mean they are “suitable substitutes” for a patch clamp. The Examiner is referred to Figures 10 and 14 of the application which illustrate examples of the gradual changes made possible with the claimed method. Prior to the present invention, no one thought that external electrodes could be used to set transmembrane potential to a desired level, and Connolly is consistent with this conventional outlook on the effects of extracellular electrodes.

The remaining prior art of record does not cure either of the above-mentioned deficiencies. Thus, Applicants respectfully request the Examiner’s rejection of independent amended Claim 1 be reconsidered and withdrawn. Claims 2-7 are dependent on amended Claim 1. It is respectfully submitted that these claims are patentable for at least the same reasons as set forth above with regard to amended independent Claim 1.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or

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other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the previous Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If any issues remain that could be resolved by telephone, the Examiner is invited to call the undersigned directly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: _____

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